

Risk Factors of Survival in Elderly Gastric Cancer Patients after Gastrectomy

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Abstract

Background

There are few studies on risk factors of surgical mortality in elderly gastric cancer (GC) patients with curative gastrectomy. This study aimed to investigate the tumor-specific survival (TSS) and associated risk factors in this elderly GC patients and help to enhance perioperative care in high risk GC patients.

Methods

Elderly GC patients (≥ 70 years) who underwent gastrectomy between January 2013 and December 2017 in Peking Union Medical College Hospital were included. Clinicopathologic characteristics, nutritional assessment (Nutritional risk screening 2002, NRS2002, prognostic nutrition index, PNI), comorbidities (Charlson Comorbidity index, CCI), operation and survival data by regular follow-up were collected. Receiver Operating Characteristic (ROC) analysis was used to extract the best cut-off point. Impact of factors on TSS was assessed using Cox proportional hazards model.

Results

Univariate analysis determined multiple variables as risk factors of TSS mainly including BMI (Hazard ratio [HR]=0.886; 95%CI, 0.824-0.952; $p=0.001$), CCI ≥ 3 (HR=2.834; 95%CI, 1.258-3.711; $p=0.005$), ICU admission (HR=1.733; 95%CI, 1.077-2.788; $p=0.024$), NRS2002 score ≥ 5 (HR=2.331; 95%CI, 1.448-3.753; $p=0.000$), preoperative PNI <45 (HR=2.058; 95%CI, 1.273-3.327; $p=0.003$). Best cut-off BMI point was 20.65 kg/m² by ROC curve. Multivariate analysis showed that BMI ≤ 20.6 kg/m² (HR=2.297; 95%CI, 1.362-3.874; $p=0.002$), postoperative ICU admission (HR=1.965; 95%CI, 1.171-3.300; $p=0.011$) and TNM staging (Stage II, HR=5.560, 95%CI, 1.591-19.426, $p=0.007$; Stage III, HR=16.202, 95%CI, 4.991-52.591, $p=0.000$) were significantly associated with TSS.

Conclusions

Preoperative BMI <20.6 kg/m², postoperative ICU admission and TNM stage are strong risk factors of TSS in elderly GC patients after gastrectomy. The need of comprehensive evaluation and nutrition support are urgent, particularly for the elderly GC patients.

Background

Gastric cancer (GC) ranks fifth of morbidity and third of cancer-caused mortality among malignancies worldwide[1] and has higher prevalence in East Asian countries [2]. Cases of GC increase with growing age and peak incidence occurs in the seventh decade of life making GC a disease of the elderly [3–5]. Generally, conditions of disease in elderly GC patients show more complexity and severity, including frail resulted from comorbidities and malnourishment [3, 6] high risk of surgical complications [7, 8], as well as shorter life expectancy comparing to the young population.

Systemic treatment for GC is multimodalities based on surgery and adjuvant therapy in accordance with the staging of cancer. Several studies showed that elderly GC patients after gastrectomy had significant lower survival or survival improvement compared to relatively young patients [9–13], indicating age may have some impact on surgical benefit of survival. However, some studies demonstrated that non-significant surgical complications [11, 12, 14] and mortality in elderly GC patients after gastrectomy [14]. Consequently, age has never be a determined factor or an absolute cut-off point depriving resectable GC from surgical indications in treatment guidelines [15, 16].

However, elderly GC patients with gastrectomy potentially have higher risk of surgical and medical morbidity and mortality given the research facts that elderly patients have reduced physiological functions and age-related changes of pharmacodynamics can lead to increased toxicity with doses established in younger patients [6, 17]. In recent years, clinicians are trying to develop validated risk models for operative complications and mortality after gastrectomy [18–20], which may be more beneficial in elderly GC population. Besides, good quality of life (QoL) is as important as survival in elderly GC patients, which in fact is poorly assessed in current studies and should raise increasing attention [21]. We aimed to determine various risk factors of tumor-specific survival (TSS) and help to improve the safety and efficacy of gastrectomy in elderly GC patients.

Methods

Participants and Study Design

Patients from January 1st, 2013 to December 31st, 2017 admitted to Peking Union Medical College Hospital and diagnosed as gastric cancer were included in our study. Inclusion criteria are (1) age \geq 70 years; (2) selective curative gastrectomy (R0); (3) confirmed diagnosed as gastric adenocarcinoma by postoperative pathology report. And patients with emergency surgery, or combined with other malignancies, or clinicopathologic data are partially missing were excluded. We define age \geq 70 years as “elderly” in this study and all clinicopathologic data were collected respectively (Fig. 1). Most of the patients were followed regularly in clinic and some were followed by phone calls. The protocol of this retrospective study was reviewed and approved by Institutional Review Board of Peking Union Medical College Hospital as a quality improvement project considering the retrospective nature of the present study design.

Demographics and Clinical Assessment

We collected the clinicopathologic data including gender, age, body mass index (BMI), history of smoking, preoperative high sensitivity C-reactive protein (hsCRP), ASA (American society of anesthesiologists) score, perioperative blood transfusion, Charlson Comorbidity index (CCI) score, history of neoadjuvant chemotherapy, tumor differentiation grade and TNM staging based on postoperative pathology. Age and BMI were defined at the time of surgery. CCI score is a commonly used tool to evaluate comorbidities of the patient, especially in the elderly [22, 23].

Preoperative Nutritional Assessment

BMI is a useful variable to assess general nutrition, defined as weight (kg)/ square of height (m). Other variables evaluating nutrition status including percentage of weight loss (%), Nutritional risk screening (NRS2002) score, prognostic nutrition index (PNI), serum level of hemoglobin, albumin and prealbumin. Preoperative weight loss $\geq 5\%$ was defined the condition where losing at least 5% of total body weight within 12 postoperative months. NRS 2002 is a recommended tool to screen surgical patients' nutritional risk [24], and PNI is a potentially cancer survival-related nutrition variable and has proved in some studies [25, 26].

Surgical Data Collection and Outcomes

Diagnose and treatment principles were based on Chinese guidelines for diagnosis and treatment of gastric cancer (2011 edition) [27] and Japanese gastric cancer treatment guidelines (version 4, 2014) [15]. Pathologic staging was evaluated by 7th Union for International Cancer Control & American Joint Committee on Cancer (UICC&AJCC) staging system of gastric cancer [28]. We collected surgical data including approaches of gastrectomy, dissection area of stomach, dissection area of perigastric lymph nodes, combined resection of organs, duration of operation, volume of intraoperative blood loss, ICU admission and perioperative blood infusion. Criteria for ICU admission are: (1) Postoperative requirement for hemodynamic monitoring and frequent nursing care; (2) High risk of postoperative respiratory complications requiring mechanical ventilation, such as patients with chronic obstructive pulmonary disease; (3) Cardiac functions evaluated by cardiologist as high risk and need for fluctuant monitoring and dose adjustment. Clinical outcome was 5-year TSS, defined as time intervals between the date of operation and the date of cancer-related death.

Statistical Analysis

SPSS 22.0 (IBM, Chicago, IL) were used to perform data analyses. Discrete variables were expressed as mean \pm standard deviation (mean \pm SD) or medians with interquartile range (IQR). Categorical variables were described as number and percentage (n, %). Univariate comparisons were assessed using the Chi-squared, Fisher exact or Wilcoxon rank-sum test as appropriate. Univariate and multivariate analysis was performed by Cox regression model. Factors with P near or less than 0.1 in the univariate analysis were included in the multivariate model. Receiver Operating Characteristic (ROC) analysis was used to extract the best cut-off point. Survival adjusted for censoring was calculated using the Kaplan–Meier method and medians compared using the log-rank test. The impact of various factors on TSS was assessed using a Cox proportional hazards model. P value less than 0.05 is regarded as statistical significance.

Results

Multifaceted Variables of Participation

In our GC database of total 1446 consecutive patients, 290 patients were into the final analysis. Characteristics of the included patients categorized into clinicopathologic, nutritional and surgical features are summarized respectively (Tables 1, 2 and 3). Among the 290 elderly GC patients, 77.6% were male and the average age was 74.7 ± 3.6 years. Over two-thirds (67.2%, 195/290) of the patients had locally advanced GC. 38.6% (112/290) had the history of ICU admission after the operation, one third (33.0%, 86/261) had elevated preoperative hsCRP level (≥ 3 mg/L), and 15.2% of all participants received neoadjuvant chemotherapy with at least 4-week rest preoperatively (Table 1).

Table 1
Clinicopathologic variables as potential risk factors for 5-year TSS

Clinicopathologic variables	N (%) or mean \pm SD	Univariate analysis	
		HR	95%CI P value
Gender	225 (77.6)	1.202	0.657–2.201 0.551
Male	65 (22.4)		
Female			
Age (years)	74.7 \pm 3.6	1.080	1.014–1.151 0.017
Smoke history	104 (35.9)	1.300	0.802–2.108 0.287
Yes	186 (64.1)		
No			
Neoadjuvant chemotherapy	44 (15.2)	0.820	0.407–1.654 0.579
Yes	246 (84.8)		
No			
CCI score	38 (13.1)	1.237	0.632–2.421 0.534
≥ 3	252 (86.9)		
0–2			
ASA class	121 (41.7)	1.128	0.689–1.847 0.632
≥ 3	169 (58.3)		
1–2			
Pre-op hsCRP level (mg/L)	86 (33.0)	1.749	1.047–2.924 0.033
≥ 3	175 (67.0)		
<3			
ICU admission	112 (38.6)	1.733	1.077–2.788 0.024
Yes	178 (61.4)		
No			
Peri-op blood transfusion	78 (26.9)	1.480	0.884–2.476 0.136
Yes	212 (73.1)		
No			
Tumor differentiation	181 (62.4)	0.799	0.471–1.353 0.403
Poor	87 (30.0)	0.531	0.165–1.709 0.288
Moderate	22(7.6)		
Well			
TNM stage	95 (32.8)	4.233	1.534–11.625 0.005
I	73 (25.2)	12.593	4.999–31.727 0.000
II	122 (42.0)		
III			

TSS, tumor-specific survival; CCI, Charlson comorbidity index; ASA, American society of anesthesiologists; pre-op, preoperative; hsCRP, high sensitivity C-reactive protein; ICU, intensive care unit; TNM, tumor node and metastasis.

Table 2
Nutritional variables as potential risk factors for 5-year TSS

Nutritional variables	N (%) or mean ± SD	Univariate analysis	
		HR	95%CI P value
BMI (kg/m ²)	23.1 ± 3.3	0.886	0.824–0.952 0.001
Pre-op weight loss ≥5% <5%	100(34.5) 190(65.5)	1.962	1.216–3.167 0.006
NRS2002 score ≥5 3–4	101 (34.8) 189(65.2)	2.331	1.448–3.753 0.000
Pre-op anemia Yes No	97 (33.4) 193 (66.6)	1.789	1.110–2.884 0.017
PNI score <45 ≥45	96(33.1) 194 (66.9)	2.058	1.273–3.327 0.003
Pre-op albumin (g/L) <35 ≥35	51 (17.6) 239 (82.4)	2.161	1.258–3.711 0.005
Pre-op prealbumin (mg/L) <200 ≥200	117(42.1) 161(57.9)	2.426	1.485–3.965 0.000
TSS, tumor specific survival; BMI, body mass index; Pre-op, preoperative; NRS2002, nutritional risk screening; PNI, prognostic nutrition index.			

Table 3

Surgical variables as potential risk factors for 5-year tumor-specific survival

Surgical variables	N (%)	Univariate analysis	
		HR	95%CI P value
Approach	114 (39.3)	0.362	0.049–2.679 0.320
Laparoscopic surgery	13 (4.5)	1.385	0.840–2.282 0.202
Conversion	163 (56.2)		
Open surgery			
Gastric dissection	83(28.6)	1.479	0.894–2.445 0.127
Total	207 (71.4)		
Partial			
Lymph node dissection	191 (65.9)	1.296	0.763–2.202 0.337
D2	99 (34.1)		
< D2			
Combined resection of organs	22 (7.6)	1.480	0.676–3.242 0.327
Yes	268 (92.4)		
No			
Operation duration (min)	69 (23.8)	1.219	0.711–2.089 0.472
≥240	221 (76.2)		
<240			
Intraoperative blood loss (ml)	42 (14.5)	1.668	0.925–3.005 0.089
≥400	248 (85.5)		
<400			

Regard to the nutritional assessment, patients with preoperative weight loss $\geq 5\%$, NRS2002 score ≥ 5 and PNI < 45 accounted for over one third respectively (34.5%, 100/290; 34.8%, 101/290; 33.1%, 96/290; Table 2), indicating at least 1/3 of all elderly GC patients had high nutrition risk. And preoperative lab showed 33.4% had anemia, 17.6% had hypoalbuminemia (< 35 g/L) and 42.1% had low serum level of prealbumin (< 200 mg/L). More than half of the patients (56.2%, 163/290) underwent traditional open surgery, 39.3% (114/290) underwent laparoscopic surgery and 4.5% (13/290) had the conversion from laparoscopic to open procedure. 28.6% of the patients received total gastrectomy, and others had proximal or distal gastrectomy. Almost 2/3 (65.9%) had D2 lymphadenectomy and 7.6% had combined resection of organs (Table 3).

Risk Factors of Survival by Univariate Analysis

In our elderly GC cohort, 290 patients had follow-up and 41 were lost during the postoperative follow-up. The median follow-up time was 31 (0–77) months. 86 patients died during the follow-up, and 68 patients are tumor-related recurrence or metastasis. The postoperative 1-year, 3-year and 5-year tumor-specific survival (TSS) was 93.7%, 75.9% and 65.1%, respectively. Univariate analysis determined multiple variables as risk factors of TSS including age (hazard ratio [HR] = 1.08; 95% confidence intervals [CI], 1.014–1.151; $p = 0.017$), preoperative hsCRP ≥ 3 mg/L (HR = 1.749; 95%CI, 1.047–2.924; $p = 0.033$), ICU

admission (HR = 1.733; 95%CI, 1.077–2.788; p = 0.024) and pathological TNM staging (Stage II, HR = 4.233, 95%CI, 1.534–11.625; Stage III, HR = 12.593, 95%CI, 4.999–31.727; Table 1).

Nutritional variables had good predictive value as BMI (HR = 0.886; 95%CI, 0.824–0.952; p = 0.001), preoperative weight loss \geq 5% (HR = 1.962; 95%CI, 1.216–3.167; p = 0.006), NRS2002 score \geq 5 (HR = 2.331; 95%CI, 1.448–3.753; p = 0.000), preoperative PNI < 45 (HR = 2.058; 95%CI, 1.273–3.327; p = 0.003), preoperative anemia (HR = 1.789; 95%CI, 1.110–2.884; p = 0.017), preoperative albumin \leq 35 g/L (HR = 2.161; 95%CI, 1.145–4.279; p = 0.018) and prealbumin < 200 mg/L (HR = 2.426; 95%CI, 1.485–3.965; p = 0.000) were individually and significantly associated with TSS (Table 2). Undoubtedly, no surgical variables were related to TSS (Table 3), which helped us to confirm the quality of our data.

Risk Factors of Survival by Multivariate Analysis

ROC curve were made and showed that 20.65 kg/m² was the best cut-off BMI point (Fig. 2A). Patients were then divided into two groups (BMI \leq 20.6 kg/m² vs BMI > 20.6 kg/m²), and Kaplan-Meier analysis showed the TSS of patients with BMI > 20.6 kg/m² was significantly better than those with BMI \leq 20.6 kg/m² (5-year TSS, 72% vs 39%, p = 0.000; Fig. 2B). Furthermore, multivariate analysis showed that BMI \leq 20.6 kg/m² (HR = 2.297; 95%CI, 1.362–3.874; p = 0.002), postoperative ICU admission (HR = 1.965; 95%CI, 1.171-3.300; p = 0.011) and pathological TNM staging (Stage II, HR = 5.560, 95%CI, 1.591–19.426, p = 0.007; Stage III, HR = 16.202, 95%CI, 4.991–52.591, p = 0.000) were significantly associated with poor 5-year TSS (Table 4).

Table 4

Potential risk factors of 5-year TSS were examined by Cox proportional hazards model.

Multi-regression analysis		
Factors	HR (95%CI)	P value
BMI (kg/m ²) \leq 20.6 $>$ 20.6	2.297 (1.362–3.874) 1	0.002
ICU admission Yes No	1.965 (1.171-3.300) 1	0.011
TNM stage I II III	1 5.560 (1.591–19.428) 16.202 (4.991–52.591)	0.007 0.000
TSS, tumor-specific survival; HR, hazards ratio; CI, confidence intervals; Pre-op, preoperative; ICU, intensive care unit; BMI, body mass index.		

Discussion

In the study, we evaluated elderly GC patients integrated with clinicopathological, nutritional and surgical variables comprehensively. 34.8% had a high prevalence of high nutritional risk (NRS score ≥ 5), which was associated with over 2-fold increase in hazards of 5-year TSS in univariate analysis. And similar findings were shown with other nutritional variables including PNI score, preoperative anemia, albumin and prealbumin levels. Multivariate analysis by Cox model demonstrated preoperative BMI ≤ 20.6 kg/m² and postoperative ICU admission were independently predictors of poor 5-year TSS (HR = 2.297; 95%CI, 1.362–3.874, $p = 0.002$; HR = 1.965; 95%CI, 1.171–3.300, $p = 0.011$, respectively).

Recent studies demonstrated that low BMI predicted increased surgical morbidity and mortality [29–31]. A study of 510 GC patient reported by Kim et al [29] showed that preoperative BMI ≤ 18.5 kg/m² was an independent poor prognostic factor of TSS in the stage I/II group (HR = 13.521; 95%CI, 1.186–154.197; $P < 0.05$) and an independent risk factor of postoperative complications in the stage III/IV subgroup (HR = 17.158; 95%CI, 1.383–212.940; $P < 0.05$). A recent meta-analysis [31] including 12 studies showed GC patients with BMI < 18.5 had higher risk of surgical complications and poorer survival. Controversially, some studies had different results [32, 33]. Lee et al demonstrated that there was no significance of 5-year TSS between preoperative low and high BMI groups (BMI < 18.5 vs BMI ≥ 25.0 , $p = 0.297$), and significances between normal and high BMI groups (BMI 18.5–24.9 vs BMI ≥ 25.0 , $p = 0.001$) in a study of 1909 GC patients [32]. Besides, they found that low BMI had significant lower overall survival (OS) compared to high-normal BMI (23.0–24.9). Interestingly, results from this study implied that traditional BMI cut-off point is not as much helpful as we expected and better BMI cut-off point probably lie between low-normal BMI (18.5–22.9). Ejaz et al reported of 775 GC patients that BMI was not related to postoperative complications or TSS or OS, but patients with underweight (BMI < 18.5 kg/m²) with preoperative low albumin (< 35 g/L) had worse OS [33]. However, baseline albumin level in low BMI group was significantly lower and small proportion (7.1%) of their cohort was classified as low BMI, indicating selection bias of surgical GC patients may exist as data was retrospectively collected.

BMI, as an easily available index, is universally used as an indicator of nutrition assessment in clinical practice and BMI < 18.5 kg/m² is the most commonly used cut-off point as underweight or malnutrition. However, no consensus about cut-off value of BMI for the elderly is achieved, and better BMI cut-off point is yet to be set up in elderly surgical patients with GC. For the first time, we verified preoperative BMI ≤ 20.6 kg/m² as an independent predictor and significantly associated with poor 5-year TSS in the elderly GC patients after gastrectomy. Since more clinicians realized that novel low BMI cut-off point might be more suitable and useful in elderly patients, Dutch definition [34] of low BMI for patients over 65 years is < 20 kg/m² and European Society of Clinical Nutrition and Metabolism definition [35] of low BMI is < 22 kg/m² for patients ≥ 70 years. Novel low BMI cut-off points were validated as valuable predictors in general hospital population [36]. Currently, very limited studies focused on this topic, and further study may validate our newly found BMI cut-off point in larger and prospective elderly GC patients with gastrectomy and may be extrapolated to other cancers.

Nutritional variables other than BMI in the present study showed predictive value of TSS in the univariate analysis. Preoperative weight loss > 5%, NRS2002 > 5 [37, 38], PNI < 45 [39], preoperative anemia, low albumin (< 35 g/L) [40, 41] and low prealbumin levels [42] are reported in several studies to be related to surgical morbidities and/or cancer survival individually or as variables of a model. Preoperative weight loss and anemia as main clinical symptoms of GC are closely related to low BMI. Intrinsic connections or crossover concepts among BMI with NRS2002, albumin with PNI, and albumin with prealbumin are probably confounders which should be eliminated by multivariate analysis methodologically. Besides, BMI probably acts as reflection of general fitness of these elderly GC patients given the fact that cancer is a chronic and consumptive disease commonly ending up with cachexia in terminal phase. Consequently, it is understandable that BMI is the only nutritional variable as risk factor of 5-year TSS in multivariate analysis.

The Charlson comorbidity index (CCI) has been proved numerously with good reliability, excellent correlation with mortality and progression-free survival (PFS) outcomes, particularly to account for the effect of age [23]. CCI is a common tool in geriatric units and helpful in assessment of concurrent diseases in elderly patients. Postoperative ICU admission often results from cardiac, pulmonary, hepatic and/or renal dysfunctions, which is common in elderly patients with more morbid illnesses. ICU admission might be closely related to complex comorbidities in elderly GC patients and as an independent predictor of TSS (HR = 1.965; 95%CI, 1.171-3.300). Also, we found TNM staging (stage II, HR = 5.56, 95%CI, 1.59–19.42; stage III, HR = 16.20, 95%CI, 4.99–52.59, $p < 0.01$) were associated with TSS significantly as widely known.

Elderly GC patients have higher nutritional risk, more comorbidities and increased mortality. When it comes to surgery for patients with early or locally advanced GC patients, multiple factors result in high surgical morbidities and mortality. However, chronological age alone is not an independent factor to withhold curative or palliative treatment from elderly GC patients, and cofactors including physical and physiological functions, mental and even socioeconomic status have to be considered [3]. Thereafter, several tools are recommended to assess elderly GC patients, such as comorbidity indices (CCI), nutrition indices (NRS2002) and prognostic indices for survival (PNI). Recently, GO2 trial [43] including 514 elderly and/or frail patients with advanced gastroesophageal (GO) cancer had preliminary results, showing that 60% dose of standard regimens had non-inferiority PFS (HR = 1.10; 95%CI, 0.90–1.33) compared to standard regimens (Oxaliplatin 130 mg/m² d1, Capecitabine 625 mg/m² bd d1-21, q21d), as well as less toxicities and better overall treatment utility (OTU), a novel patient-centered endpoint [44]. Previously, results of 321GO demonstrated favoring a doublet regimen over single agent or triplet chemotherapy in 55 elderly or frail advanced GO patients as a randomized phase II and feasibility study [6]. And both implied a common refrain in some cancer treatment is “less may be more”, which probably enlighten us whether elderly and/or frail GC patients with surgical indication could have a shrink conversion from current D2 lymphadenectomy as the standard and curative approach, or could the adjuvant chemotherapy regimens be simple or reduced dose.

There are some limitations in the present study. Firstly, the retrospective nature of the study design lowers the quality of data and sample size is relatively small. Secondly, we did not collect surgical morbidity data here and QoL was not assessed postoperatively, although we recognized the significance of it to elderly GC patients. What's more, it is a single center study from China, we should be cautious when generalizing to populations whether in other countries or with other cancers. To the best of our knowledge, it is for the first time that an exact BMI cut-off value ($< 20.6 \text{ kg/m}^2$) was determined as risk factor of poor 5-year TSS in elderly GC patients. Future studies may have further comprehensive assessment of elderly surgical patients and probably use novel tools, such as OUT [43, 44].

Conclusions

In conclusion, we found that preoperative BMI $< 20.6 \text{ kg/m}^2$, postoperative ICU admission and TNM stage are strong risk factors of tumor-specific survival in elderly GC patients after gastrectomy. These findings may help to evaluate elderly GC patients optimally and to identify those high-risk patients with gastrectomy. The need of comprehensive evaluation and nutrition support are urgent, particularly for the elderly GC patients.

Abbreviations

GC: Gastric cancer; TTS: tumor-specific survival; NRS2002: Nutritional risk screening 2002; PNI: prognostic nutrition index; CCI: Charlson Comorbidity index; HR: hazard ratio; CI: confidence intervals; ICU: intensive care unit; BMI: body mass index; QoL: quality of life; hsCRP: high sensitivity C-reactive protein; ASA: American society of anesthesiologists; IQR: interquartile range; ROC: receiver operating characteristic; PFS: progression-free survival; GO: gastroesophageal; OTU: overall treatment utility

Declarations

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Authors' contributions

XL and JCY designed the study, XL mainly set up the database and ZQM, ZGX and WMK had quality control of data and algorithms. XL and JCY did data analysis and interpretation. XL and ZGX drafted the manuscript. All authors reviewed the final version of manuscript and agreed to submit.

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Availability of data and materials

The datasets used and analyzed during the current study are available from the corresponding author on reasonable request.

Ethics approval and content to participate

The protocol of this retrospective study was reviewed and approved by Institutional Review Board of Peking Union Medical College Hospital as a quality improvement project considering the retrospective nature of the present study design.

Content for publication

Not applicable.

Competing interests

The authors declared that they had no competing interests.

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Figures

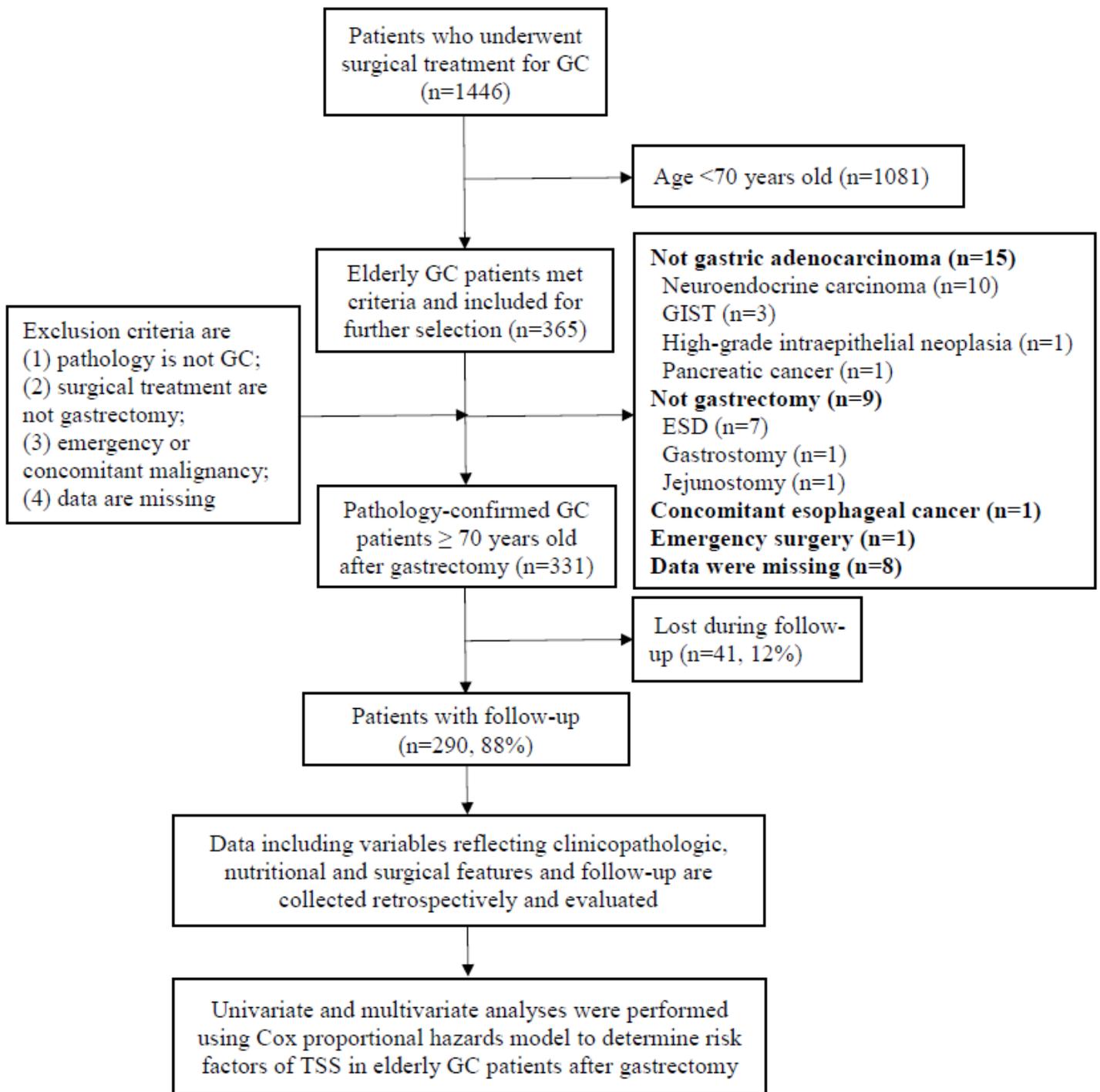
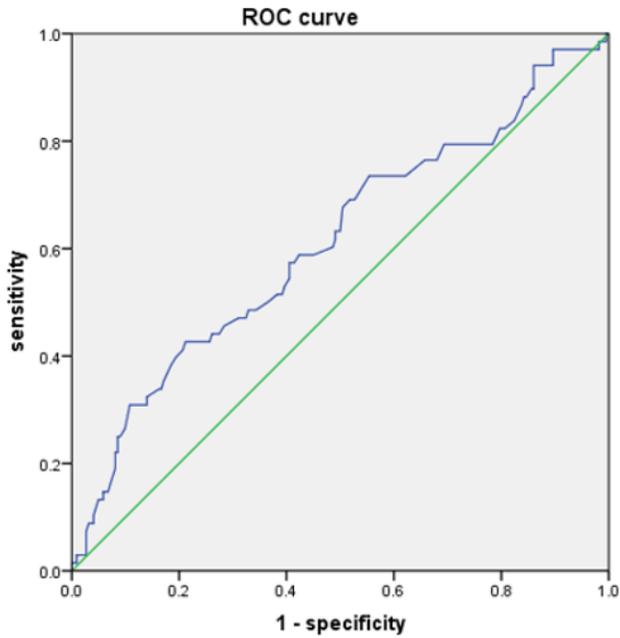
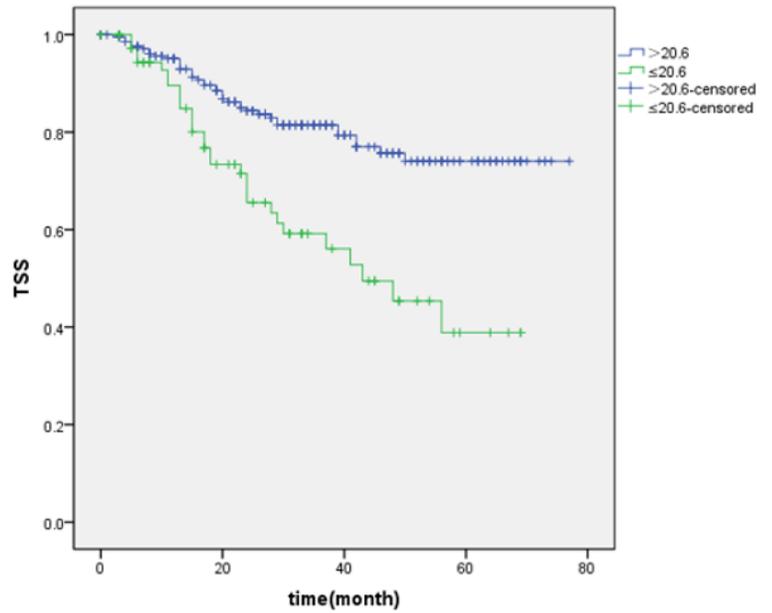


Figure 1

Diagram of the study design.

Fig. 2A**Fig. 2B****Figure 2**

A ROC curve of relationship between BMI and TSS. The AUC was 0.611 ± 0.041 , 95%CI 0.531-0.691, $p=0.006^*$. Maximal Youden index was 0.21 as sensitivity value was 0.426, specificity was 0.788 and the corresponding BMI cut-off point was 20.65 kg/m². Fig. 2B TSS between low BMI and high BMI group. Novel cut-off point, 20.6 kg/m², was used in Kaplan-Meier method making TSS curve of the two groups. Log-rank test was performed and χ^2 was 16.271, $P=0.000$. ROC, receiver operating curve; BMI, body mass index; AUC, area under curve; CI, confidence interval. TSS, tumor-specific survival.